Editorial

European Respiratory Society International Congress 2018: insights from the paediatric assembly

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The ERS International Congress 2018 represented the theatre, for researchers with an interest in respiratory medicine, to feature their work to the researchers' community. In this article, we provide the insight from the paediatric assembly, summarizing the results of the highest quoted abstracts presented at the meeting. We grouped the reviewed abstract in different categories as follows.

Lung conditions in premature infants

Premature deliveries are increasing in absolute numbers internationally. With the new international working schemes and the travel ease, there are an increasing number of mothers who deliver their premature babies in other than their home origin. Neonatal transfers by plane both in short-lasting and transatlantic flights are increasing in number. The inflight hypoxia is a common complication and tests to predict the amount of oxygen required during each flight have been developing. The hypoxia challenge test (HCT), that has been validated in adults and older children, was assessed in 30 preterm infants (median age of 29.1 weeks of gestation) with a corrected age of 22.5 (–1.7 to 50.9) weeks in a total of 50 flights. Inflight responses and additional oxygen requirements were inconsistent with the results of the HCT and therefore HCT cannot be suggested as a good predictor of inflight oxygen responses in preterm babies (1).

Premature birth consists of the main risk factor for chronic lung disease development. In view of the increased numbers of premature infants who survive, predicting and preventing chronic lung disease constitutes an important public health focus. Pulmonary inflammation precipitated and exacerbated by proinflammatory mediators (IL-1b, IL6 and IL8), consists of the core of chronic lung disease. By stimulating cell lines (A549 and Beas2B cells) with neat and a caspase activation domain (ASC)-depleted bronchoalveolar lavage, it was shown that ASC-modulation could directly affect proinflammatory responses in an Nfkb suggested pathway. This observation can potentially lead to important therapeutic implications (2).

Ureaplasma-triggered respiratory infections have more adverse outcomes in preterm infants as a risk factor for bronchopulmonary dysplasia but later pulmonary outcome is still unknown. In a prospective, multicentre, randomised controlled trial, 121 ureaplasma-positive preterm infants were randomly assigned to azithromycin or placebo. Parental completed questionnaires assessing clinical outcomes at 6 and 12 months post treatment were analysed. Azithromycin was shown to improve survival by reducing respiratory morbidity in this group of preterm infants (3).

Low variability of tidal volume (VT) and capnographic indices in preterm infants is an indication of impaired lung function. In a prospective cohort-study including 133 unsedated preterm infants, it was investigated whether impaired lung function measurements could be associated with subsequent rehospitalization, episodes of wheeze, or inhalation therapy. Impaired lung function measurements were negatively associated with rehospitalization during infancy. Including near term variability of tidal breathing parameters to BPD classification improves prediction of rehospitalization in infancy (4).

Research work around asthma

Paediatric asthma is a heterogeneous condition and therefore management should be usually guided by the

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phenotype and the responses. Difficult, resistant to steroids treatment asthma requires further investigation. In a multicentre European study (U-BIOPRED) preschool and school-age children with moderate and severe asthma were gene tested by gene network analysis. The results did not highlight big differences. The mitochondrial oxidative stress showed to have a role in early onset severe asthma. This pathway deserves further investigation (5).

It has been shown that asthmatic airways are characterised by remodelling. MicroRNAs play a significant role in regulating inflammatory responses at post-transcriptional stage. In an asthmatic mouse model of OVA induced asthma, it was highlighted that miR-133a has the potential to regulate the expression of α-SMA through PI3K/AKT/mTOR signalling. This is novel therapeutic pathway that requires further investigation in the future (6).

Childhood obesity consists of a major public health problem. In a Dutch birth cohort study, 4,435 children were assessed and it was shown that peak weight velocity and body mass index at adiposity peak were associated with lower lung function measurement at age 10 years but not asthma, independently of child's current weight status. Further research utilising broader outcome measures might clarify whether there is a stronger association between obesity and asthma incidence (7).

Use of analgesics during pregnancy is very common and it was suggested to be associated with child asthma. A Swedish retrospective study considered this association by 492,999 mother-child pairs identified from Swedish registers and the incidence of childhood asthma at the age of 2–6 years. It was shown that any type analgesic use in pregnancy was associated with childhood asthma but sibling analysis found no increased risk for asthma in those exposed prenatally to analgesics compared to their non-exposed siblings. This association needs further seeking as confounders such possible maternal medical condition underlying might bias these findings (8).

Research work around cystic fibrosis

In cystic fibrosis it has been shown that colonisation of the lower airways with bacteria starts early in the disease history. Staphylococcus Aureus and Haemophilus influenza are very early detected in sputum samples and Pseudomonal aeruginosa follows as the disease progresses. In a prospective cohort-study, 310 infants diagnosed with cystic fibrosis during new-born screening underwent CT scans at 3–6 months, 1 year, and annually up to 6 years of age. Bronchoalveolar lavage samples were obtained from these children and they detected P. aeruginosa, H. influenza, S. aureus, and Aspergillus species all from early infancy. The detection of the above pathogens correlated as independent factors significantly with the disease progression (associated lung function deterioration) (9).

It is well established knowledge that lungs of patients with cystic fibrosis are microbiome-rich. However, all children's lungs are hosting a plethora of pathogens. Data from 106 preschool children with cystic fibrosis compared to 50 controls highlighted a lower diversity, and different relative abundance at phylum, family and genus level. The type of pathogens (Staphylococcus and Pseudomonas were more abundant in cystic fibrosis patients) and proinflammatory and neutrophil mediated inflammatory responses were significantly impaired. The effect of antibiotics on microbiome changes is minimal. Further research is required to define other possible mediators of microbiome changes in cystic fibrosis (10).

Research work in respiratory infections

Viral-bacterial co-infections consist of the most common triggers for lower respiratory tract infections in childhood. The mechanisms underlying as well as whether viral infections precipitate bacterial and vice versa, have not been studied thoroughly. Primary bronchial epithelial cells from healthy non- infected children were cultured using a closer to the "*in vivo*" model (air liquid interface cultures) and infected with respiratory syncytial virus (RSV) and nontypeable Haemophilus influenza in different sequences. It was shown that infection with RSV precipitates nontypeable Haemophilus influenza colonisation, the reverse though does not increase the risk of RSV infection. This is an observation that could potentially add to the importance of viral infections in the epithelium changes in children's lungs (11).

Complicated intrathoracic tuberculosis is a very severe presentation of the disease and a timely diagnosis is very important. In a prospective study, 132 children enrolled (median age 18 months), treated for tuberculosis for median 5.5 days, had either a bronchoalveolar lavage culture or GeneXpert testing on the bronchoalveolar lavage. It was shown that GeneXpert testing in complicated tuberculosis increased the diagnostic yield by 29% as compared to the culture method. This is an important observation for a non-common but severe presentation of tuberculosis (12).

Acute bronchiolitis is one of the most common

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respiratory infections during infancy. RSV is the most frequently detected pathogen in bronchiolitic infants. RSV subtype-A is thought to have a more severe clinical course than RSV-B in bronchiolitis. The RSV viral load as well as the expression of IFN-stimulated genes such as MxA and ISG56 were detected in nasopharyngeal washes from 96 infants with bronchiolitis (NA1: 50 and ON1: 46). An elevated level of IFN-stimulated genes was observed in infants infected with RSV-A genotype NA1 that caused a more severe bronchiolitis course, while ON1 showed a higher viral load. These findings represent an important observation for vaccine development (13).

Miscellaneous research

The mesenchyme gives rise to multiple distinct cell lineages in the mature respiratory system, including smooth muscle cells of the airway and vasculature, vascular endothelial cells, and parenchymal fibroblasts. It is of increased significance to understand the diversity in mesenchymal derived cells in the human lung. This study attempted to identify these changes by using RNAseq of human foetal lung cells, to characterize cellular phenotypes in the pseudoglandular (11.5 weeks) and early canalicular (18.5 weeks) stages of human lung development. Specific diversion in mesenchymal lineages as it refers to membrane molecules expression and signalling is taking place quite early in lung development. The question then is can we interfere and how (14).

Childhood interstitial lung disease (chILD) is encompassing more than 200 rare disease entities. There is no consensus referring to the management of these diverse conditions. A chILD-EU registry study was initiated in 2012 and included children with ILD from 13 countries, analysis funded by COST Action CA16125 ENTeR-chILD. The three most frequent medications prescribed at study baseline or within a period of 3 months were analysed via multivariate logistic regression models. Corticosteroids were found to be the most frequently used medications. There are significant differences in use of medications across Europe. It is essential that Europe engages in an evidence-based manner to eliminate the differences that may adversely affect the quality of treatment these patients receive (15).

Alveolar capillary dysplasia with misalignment of the pulmonary veins (ACD/MPV) is a rare disorder with increased morbidity. A quick diagnostic tool is missing and is of great importance. This study developed a non-invasive genetic test based on targeted ion torrent next generation sequencing (IT NGS) that detects genetic alterations in the FOXF1 locus. It is a promising advance in this field and of great importance to be tested in greater number of patients (16).

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Footnote

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